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Type D personality and vulnerability to adverse outcomes in heart disease

■ ABSTRACT

General distress, shared across depression, anxiety and anger, partly accounts for the link between mind and heart. The type D (distressed) personality profile identifies individuals who are particularly vulnerable to the adverse effect of general distress. Type D individuals frequently experience negative emotions and are socially inhibited. This profile is more stable than that associated with episodes of clinical depression and describes the chronic nature of distress in some patients. Type D may also partly account for the effect of emotional distress on cardiac prognosis. Type D is associated with a threefold increased risk of adverse cardiovascular outcomes, even after adjustment for depression. This relationship is less obvious in patients with heart failure. Plausible pathways linking type D to cardiovascular complications include hypothalamic-pituitary-adrenal-axis hyperreactivity, autonomic and inflammatory dysregulation, and increased oxidative stress. Research needs to further clarify these pathways and investigate whether type D patients may benefit from closer monitoring of risk factors and a personalized approach to behavioral intervention. The DS14 is a brief, well-validated measure of type D that could be incorporated into clinical research and practice to identify high-risk patients.

Depression has been studied extensively in relation to cardiovascular disease.¹⁻³ In addition to depression, anger⁴ and anxiety⁵ also may promote coronary artery disease (CAD), suggesting that emotional distress in general may be related to increased cardiovascular risk. Evidence indicates that the general distress shared across depression, anger, and anxiety predicts CAD, even after controlling for each of these specific negative emotions.⁶

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■ THE CONCEPT OF TYPE D PERSONALITY

Lately, there is a renewed interest in broad individual differences in general distress and heart disease.⁷ Since psychologic factors often cluster together in individual patients, biobehavioral research may benefit from the identification of discrete personality subtypes.⁸ This focus on the identification of psychologically vulnerable patients who are at increased risk for adverse outcomes has led to the introduction of the *distressed*⁹ or *type D*¹⁰ personality profile in cardiovascular research. This personality construct is defined as follows:

*“The type D (distressed) personality profile refers to a general propensity to psychological distress that is characterized by the combination of negative affectivity and social inhibition.”*¹⁰

Negative affectivity, or the tendency to experience negative emotions across time and situations, is a major determinant of emotional distress in cardiac patients.^{9,10} Patients who score high on this trait frequently report feelings of dysphoria, worry, and tension. Social inhibition, or the tendency to inhibit the expression of emotions or behavior, is a major determinant of social distress.^{9,10} Patients who score high on this trait tend to avoid negative reactions from others.

Both traits define psychologically vulnerable patients and can be assessed with the type D scale (DS14).¹⁰ This brief measure consists of a seven-item negative affectivity subscale (eg, *I often feel unhappy*) and a seven-item inhibition subscale (eg, *I am inhibited in social interactions*), and has a clear two-factor structure and good reliability (Cronbach's $\alpha = .88$ and $.86$). Patients are classified as type D if they score 10 or higher on both DS14 subscales.¹⁰ The prevalence of type D personality ranges between 20% and 40% across different types of cardiovascular conditions.

The type D construct was designed for the early identification of chronically distressed patients. This article reviews (1) the risk of adverse events associated with type D, (2) the extent to which type D is

TABLE 1**Type D and risk of clinical events in cardiovascular disease patients**

| Cardiovascular disease (n) | Clinical event (follow-up) | OR/HR (95% CI) | Meta-analytic review ²³ |
|----------------------------|------------------------------|----------------------------------|------------------------------------|
| CAD | | | |
| CAD (303) ¹¹ | Total mortality (6–10 y) | OR = 4.1 (1.9–8.8)* | Included in meta-analysis |
| CAD (319) ¹² | Cardiac death, MI (5 y) | OR = 8.9 (3.2–24.7) [†] | Included in meta-analysis |
| CAD (337) ¹³ | Total mortality, MI (5 y) | OR = 4.8 (1.4–16.5)* | Included in meta-analysis |
| CAD (875) ¹⁴ | Total mortality, MI (9 mo) | OR = 5.3 (2.0–13.6) [†] | Included in meta-analysis |
| CAD (358) ¹⁵ | Total mortality, MI (2 y) | HR = 2.6 (1.1–6.0) [‡] | Included in meta-analysis |
| CAD (473) ¹⁶ | Cardiac death, MI (1.8 y) | HR = 2.2 (1.1–4.3) [‡] | Not included in meta-analysis |
| Other | | | |
| PAD (184) ¹⁷ | Total mortality (4 y) | HR = 3.5 (1.1–11.1) [‡] | Included in meta-analysis |
| CHF (87) ¹⁸ | Cardiac death, MI (6–10 y) | OR = 4.7 (1.9–11.8)* | Included in meta-analysis |
| CHF/HT (51) ¹⁹ | Mortality, rejection (5.4 y) | OR = 6.8 (1.4–30.9) [‡] | Included in meta-analysis |
| CHF (641) ²⁰ | Cardiac death (3.1 y) | HR = 1.2 (0.6–2.1) | Not included in meta-analysis |
| ICD (391) ²¹ | Ventricular arrhythmia (1 y) | HR = 1.9 (1.1–3.1) [‡] | Not included in meta-analysis |
| ICD (371) ²² | Total mortality (1.7 y) | HR = 2.8 (1.2–6.2)* | Not included in meta-analysis |

* $P < .01$; [†] $P < .0001$; [‡] $P < .05$

CAD = coronary artery disease; CHF = chronic heart failure; HR = hazard ratio; HT = heart transplantation; ICD = implantable cardioverter defibrillator; MI = myocardial infarction; OR = odds ratio; PAD = peripheral arterial disease

distinct from depression, (3) the biologic pathways of type D, and (4) the implications of the type D personality profile.

RISK ASSOCIATED WITH TYPE D

Several prospective studies from our group have examined the notion that type D patients are particularly vulnerable to adverse events (Table 1). In patients with CAD, evidence indicates that type D personality is an independent predictor of adverse events, including (cardiac) death, myocardial infarction, and need for revascularization procedures.^{11–16} In these studies, type D also emerged as an independent predictor of adverse events after adjustment for anxiety,¹¹ stress,¹³ depression,¹⁶ disease severity,^{11–16} and type of invasive treatment.¹⁴ This increased risk associated with the type D profile was observed in the broader group of patients with CAD,^{11–15} as well as in patients who survived an initial myocardial infarction.¹⁶

The relationship between type D personality and adverse events has also been investigated in other cardiovascular conditions. Type D has been associated with poor prognosis in patients with peripheral arterial disease,¹⁷ but evidence for the prognostic role of type

D in patients with chronic heart failure is mixed. In a study of patients with heart failure following myocardial infarction, type D predicted cardiac death independent of disease severity¹⁸; in a study of heart failure patients who underwent cardiac transplantation, type D was associated with early allograft rejection and increased mortality.¹⁹ However, type D was not associated with cardiac death in a recent, larger heart failure study.²⁰ The link between psychologic factors and heart failure is complex³ and may be less obvious than the type D-CAD link.²⁰ Type D has also been associated with the occurrence of life-threatening arrhythmias following implantable cardioverter defibrillator (ICD) treatment,²¹ and it has been shown to predict an increased risk for mortality in ICD patients, independent from shocks and disease severity.²²

The wide range in odds ratios and confidence intervals indicates disparity in data across these type D studies (Table 1). We recently performed a meta-analysis of prospective studies between 1996 and 2009 to provide a more reliable estimate of the risk associated with type D. In this analysis, type D was associated with a threefold increased risk of adverse events²³; the confidence interval of this pooled odds ratio ranged

from 2.7 to 5.1. In addition, type D personality was associated with a threefold increased risk (range, 2.6 to 4.3) of emotional distress over time.²³ From the recent studies that were not included in this meta-analysis, one reported negative findings²⁰ and three others positive findings^{16,21,22} on the risk associated with type D.

■ COMPARING DEPRESSION AND TYPE D

Many studies report on depression and cardiac disease,^{1–3} but both conceptual differences and clinical evidence indicate that type D and depression are distinct forms of distress (**Table 2**). Conceptually, type D focuses not only on depressive affect but also on the general distress shared across negative emotions,¹⁰ and it is based on the notion that social inhibition modulates the effect of negative emotions on cardiac prognosis.²⁴ While depression refers to an episodic distress factor (patients may go in and out of depressive episodes), the type D construct focuses on an underlying factor that predisposes patients to more chronic forms of distress.⁸

Clinical evidence shows that, after adjustment for depression, type D remained a predictor of adverse cardiac events in CAD.^{16,24,25} Following ICD implantation, anxious type D patients were at risk of ventricular arrhythmias, whereas depression did not predict arrhythmias.²¹ Type D also exerts an adverse effect on patients' health status following coronary bypass surgery,²⁶ heart failure,²⁷ or myocardial infarction,²⁸ adjusting for depressive symptoms. Type D is related to biomarkers of increased stress levels independent of depression^{29–31} and, unlike depression, type D is not confounded by the severity of cardiac disorder.³²

Following myocardial infarction, only one of four distressed patients met criteria for both type D and depression; most had one form of distress but not the other.³² Research in healthy³³ and in cardiac³⁴ populations confirmed that items from depression and type D scales reflect different distress factors. After adjustment for depression at baseline, type D also predicted the incidence,³⁵ persistence,³⁶ and severity^{37,38} of depression and anxiety. However, these findings do not imply that depression and type D are antonymous perspectives or that one perspective is better than the other in predicting outcomes; rather, we would like to argue that both constructs represent complementary perspectives that have added value.²³

■ BIOLOGIC PATHWAYS OF TYPE D

A number of biologic pathways have been suggested to explain the effect of type D (**Table 3**). Some have suggested dysregulation of the hypothalamic-

TABLE 2

Type D and depression are different forms of distress in cardiovascular disease patients

| Conceptual differences | |
|-------------------------|---|
| Emotional | Type D focuses on general distress shared across negative emotions (anxiety, irritability, and others ¹⁰) in addition to depressive affect |
| Social | Social inhibition is a factor in type D that may moderate the expression of emotions and behaviors in social interaction ²⁴ |
| Duration | Emotional and social distress is a chronic factor (≥ 2 years) in type D, whereas it is an episodic factor (< 2 years) in depression ^{8–10} |
| Cardiovascular outcomes | |
| Clinical events | Type D personality predicts mortality and other clinical events in cardiac patients, even after adjustment for severity ¹⁶ and symptoms ^{24,25} of depression |
| Health status | Type D personality independently predicts poor health status over time in cardiac patients, above and beyond symptoms of depression ^{26–28} |
| Pathways of disease | Type D personality predicts increased oxidative stress and cortisol levels in cardiac patients after adjustment for depressive symptoms ^{29–31} |
| Psychologic outcomes | |
| Distinct diagnosis | There is only limited overlap between type D and depression classification ^{25,32} ; items in type D and depression scales reflect different distress factors |
| Depressive symptoms | Type D personality predicts the onset and persistence of depressive symptoms in cardiac patients, controlling for depression at baseline ^{35,36} |
| Anxiety symptoms | Type D personality predicts the occurrence and severity of anxiety in cardiac patients, above and beyond symptoms of depression ^{37,38} |

pituitary-adrenal axis in patients with type D personality.³⁹ In fact, type D has been associated with greater cortisol reactivity to stress in healthy individuals⁴⁰ and with higher awakening³⁰ and daytime³¹ cortisol levels in CAD patients. Autonomic dysregulation can also be inferred in type D individuals on the basis of a higher resting heart rate⁴¹ and cardiovascular hyperreactivity^{40,42} and decreased heart rate variability⁴³ in response to stress. In addition, type D has been related to reduced heart rate recovery after

TABLE 3
Potential biologic mechanisms underlying type D

| | Healthy individuals | Cardiovascular patients |
|------------------------------|---|--|
| HPA-axis dysregulation | Increased cortisol reactivity to stress ⁴⁰ | Higher CAR ³⁰ ; higher daytime cortisol ³¹ |
| Autonomic dysregulation | Higher HR ⁴¹ ; increased CV stress reactivity ^{40,42} ; decreased HRV ⁴³ | Reduced HR recovery after exercise ⁴⁴ |
| Inflammatory dysregulation | Higher concentration of CRP ⁴¹ | Increased plasma levels of TNF- α , TNFR1, TNFR2 ^{46,47} |
| Reduced number of stem cells | Decreased EPC counts associated with NA ⁴⁸ | Decreased EPC counts associated with type D ⁴⁹ |
| Increased oxidative stress | | Lower levels of Hsp70 and higher levels of XO ²⁹ |

CAR = cortisol awakening response; CRP = C-reactive protein; CV = cardiovascular; EPC = bone marrow-derived endothelial progenitor cells; HPA = hypothalamic-pituitary-adrenal; HR = heart rate; HRV = heart rate variability; Hsp70 = heat shock protein 70; NA = negative affectivity; TNF- α = tumor necrosis factor- α ; TNFR1 = soluble TNF- α receptor 1; TNFR2 = soluble TNF- α receptor 2; XO = xanthine oxidase

exercise in patients with heart failure.⁴⁴ These indices of excessive sympathetic or inadequate parasympathetic modulation of heart rate predict poor cardiac prognoses.⁴⁵

Other studies found that type D was associated with inflammatory dysregulation. In healthy adults, type D has been related to higher concentrations of C-reactive protein.⁴¹ In heart failure patients, type D is associated with increased plasma levels of the pro-inflammatory cytokine tumor necrosis factor (TNF)- α and its soluble receptors 1 and 2.^{46,47} Increased TNF- α levels may cause suppression of bone-marrow-derived endothelial progenitor cells (EPCs) that play an important role in maintaining vascular integrity. The negative affectivity component of type D has been shown to predict decreased circulating EPC counts in healthy individuals⁴⁸; another study found that these EPC numbers were reduced by more than 50% in heart failure patients with a type D personality.⁴⁹ Type D personality is also associated with an increased oxidative stress burden in patients with chronic heart failure.²⁹ Studies on genetic linkage⁵⁰ and heritability⁵¹ further support biologic underpinnings of the type D construct.

Regarding pathways that may explain the effect

of type D, some issues are of special interest. First, genetic factors contribute to stability in type D personality, but environmental factors may induce changes in type D characteristics over time.⁵¹ Hence, given this role of environmental influences over time, behavioral intervention would be feasible and useful in type D patients. Second, type D can promote heart disease indirectly through behavioral pathways. Type D has been associated with a sedentary lifestyle,^{41,52} an unhealthy diet,⁵³ and a passive coping style.^{54,55} Poor adherence to medical treatment^{56,57} and reluctance to consult clinical staff⁵⁸ may jeopardize the working relationship with type D patients in clinical care. Intervention may focus on the management of these behavioral risk factors in type D patients. Third, many of these biologic^{40–43,48,50,51} and behavioral^{41,52–54} pathways have also been documented in healthy type D individuals, which suggests that these associations cannot be explained away by the confounding effect of underlying cardiovascular disease.

CLINICAL IMPLICATIONS OF TYPE D

The findings from type D research have a number of clinical implications. Type D is associated with an increased risk of adverse events,²³ chronic distress,^{35–38} and suicidal ideation.⁵⁹ Type D may also have an adverse effect on the outcome of invasive treatment.^{14,19,21,22,24,26,60}

Type D was associated with mortality and morbidity at 9 months¹⁴ and 2 years²⁴ following coronary artery stenting, and with impaired health status 1 year following bypass surgery.²⁶ Type D also predicted mortality and allograft rejection following heart transplantation,¹⁹ and an increased risk of ventricular arrhythmia²¹ and mortality²² in ICD patients. Researchers from the Cleveland Clinic have shown that type D is a risk factor for anxiety in ICD patients.⁶⁰

Regarding the DSM-IV classification by the American Psychiatric Association,⁶¹ type D qualifies for the diagnosis “psychological factors affecting medical condition” (Section 316). In keeping with this classification, the diagnostic category type D affects (1) the *course* of cardiovascular conditions,²³ (2) the *treatment* of these conditions,^{56,57} and (3) the *working relationship* with medical staff.⁵⁸ At present, no clinical trial has examined whether intervention for distress among type D patients alters their risk for adverse events. Nevertheless, some have argued that it is plausible for type D patients to learn new strategies to reduce their level of general distress.⁶² Previous research with patients experiencing symptoms like those of type D patients suggests that psychotherapy,

social skills training, stress management, and relaxation training may reduce stress in these patients and improve their ability to express their emotions to others.⁶² Others have suggested that stress management training, including communication skills and problem-solving, may further improve the risk profile and health in cardiac patients.⁶³

It is possible that type D patients may benefit from close monitoring of their clinical condition and from aggressive management of their risk factor profile to prevent adverse clinical events. Cardiac rehabilitation is an effective approach to treating risk factors and enhancing well-being in CAD.^{63,64} A few studies have examined the effect of cardiac rehabilitation in type D patients. One study found a significant decrease in the social inhibition component of type D following cardiac rehabilitation, but there was no change in the prevalence of type D at 1-year follow-up.⁶⁵ Although the type D profile tends to remain stable during rehabilitation,^{65,66} evidence shows that type D patients who participate in cardiac rehabilitation improve in physical and mental health status.⁶⁶ Cardiac rehabilitation may also ward off further deterioration in negative affect,⁶⁷ which, in turn, has been associated with better survival in patients who participated in rehabilitation.⁶⁸ Future studies need to examine the effect of cardiac rehabilitation and other personalized approaches to treatment in type D patients.

CONCLUSIONS

General distress shared across negative emotions^{6,23} may partly account for the role of depression, anxiety, and anger in cardiovascular disorders.¹⁻⁵ Some cardiac patients are more likely to experience distress than others. Type D may identify these psychologically vulnerable patients who tend to experience general distress.²³ This propensity to general distress differs from depression, predicts adverse outcomes, is linked to plausible biologic pathways, and highlights the chronic nature of psychologic distress in some cardiac patients.

After adjustment for depression, type D remains significantly associated with an increased risk of adverse events in patients with CAD.^{16,24,25} However, this association is less obvious in patients with heart failure, and type D did not predict survival in one heart failure study.²⁰ Although initial findings suggest a number of plausible biologic and behavioral pathways, more research is needed to explain the adverse effect of type D on cardiovascular outcomes. Future research also needs to investigate whether type D

patients may benefit from close monitoring of their risk factors and a more personalized approach to behavioral and cardiac treatment.

Overall, the current understanding of type D indicates that general distress should not be ignored in the link between mind and heart, and that cardiovascular patients who have a type D personality profile are particularly vulnerable to the adverse clinical effects of general distress. The DS14¹⁰ is a brief, well-validated measure of type D that could be incorporated into clinical research and practice to identify patients who are at risk of chronic distress and poor prognosis.

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